

**FDA – AGS Workshop**  
**Washington, DC**  
**February 26, 2014**

# Hypotony as an Adverse Outcome of Minimally Invasive Glaucoma Surgery

**Gregory L. Skuta, MD**

**President and CEO**

**E. L. Gaylord Professor and Chair**

**Dean McGee Eye Institute**

**University of Oklahoma**



# Disclosure Statement

- Dr. Skuta serves on the Claims Committee and the Finance Committee of the Ophthalmic Mutual Insurance Company (OMIC)
- He has no other financial disclosures.
- He has served as an investigator for the Collaborative Normal Tension Glaucoma Study, the Advanced Glaucoma Intervention Study, the Collaborative Initial Glaucoma Treatment Study, and the Tube versus Trabeculectomy Study.
- He also has served on the Data and Safety Monitoring Committee for the Ocular Hypertension Treatment Study.

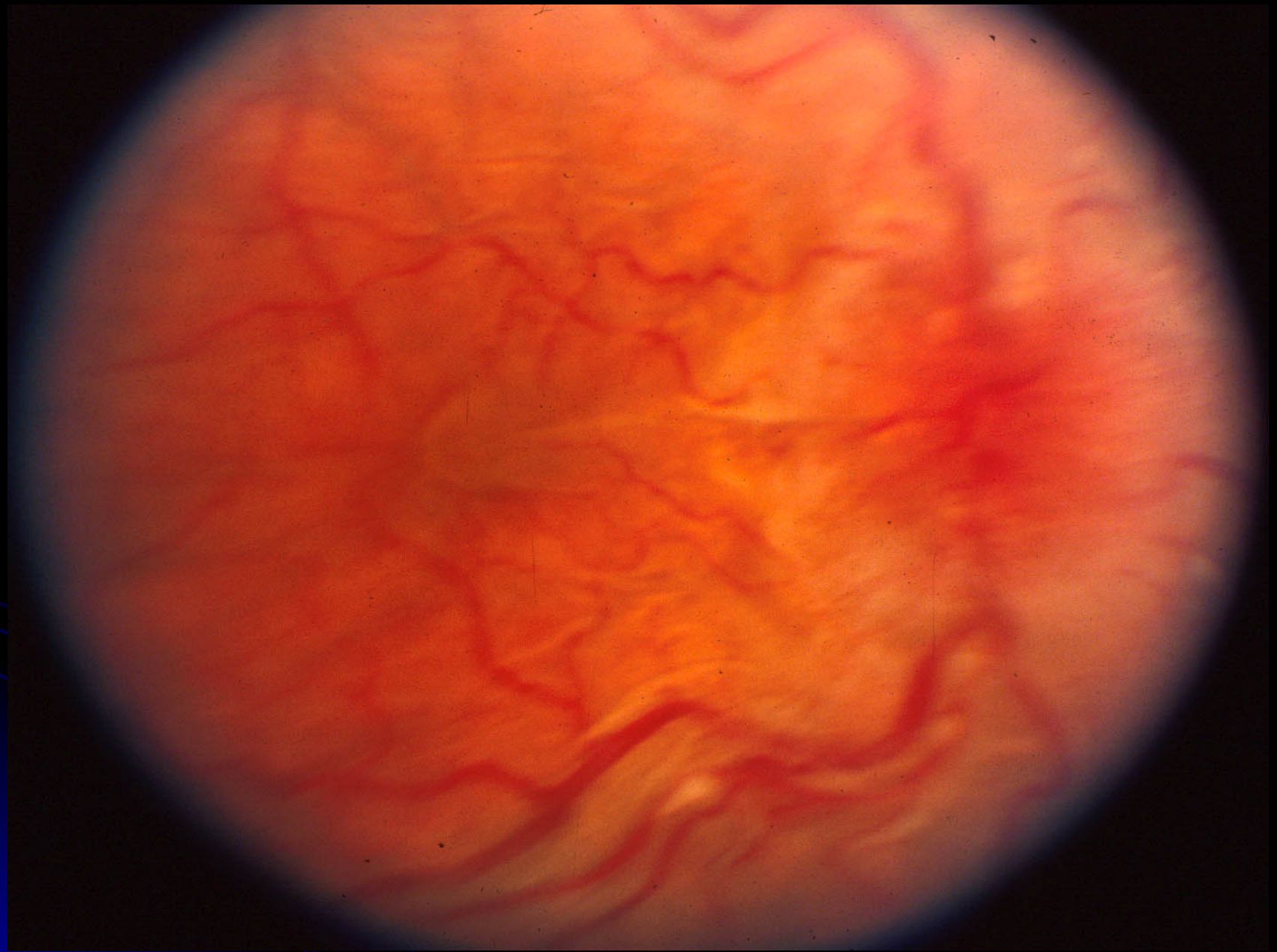
# Definition of Hypotony

- Some would define hypotony as intraocular pressure (IOP) below set level (e.g.,  $< 6$  mmHg)
- In two textbooks, Pederson defined “statistical hypotony” as IOP  $< 6.5$  mmHg (more than 3 standard deviations below mean)
- Others, including Pederson, would define “clinically significant hypotony” as IOP below which eye does not function normally
- Fannin, Schiffman, and Budenz (Ophthalmology, 2003) defined hypotony as IOP  $\leq 5$  mmHg
- Tube versus Trabeculectomy (TVT) Study: IOP  $\leq 5$  mmHg on two consecutive visits after 3 months

# Manifestations of Hypotony

- Corneal folds, edema, and astigmatism
- Shallow or flat anterior chamber
- Peripheral anterior synechiae
- Cataract
- Choroidal effusion and suprachoroidal hemorrhage
- Hypotony maculopathy:
  - Decreased visual acuity
  - Optic nerve and retinal edema/cystoid macular edema
  - Macular folds
- Some eyes with “statistical hypotony” experience none of the above
- Some eyes without “statistical hypotony” experience some or all of the above





*Courtesy of Paul Palmberg, MD, PhD*

# Risk Factors for Hypotony Maculopathy

- 228 eyes of 228 patients from BPEI with hypotony
- 81 eyes with hypotony maculopathy; 147 control eyes with hypotony alone
- Risk factors for hypotony maculopathy: young age, male gender, and myopia
- History of diabetes and choroidal effusion were associated with decreased risk for hypotony maculopathy

# Risk Factors for Hypotony Maculopathy

|              | Hyp/Mac | Hyp    | P-value |
|--------------|---------|--------|---------|
| N            | 81      | 147    |         |
| Mean age(y)  | 50.5    | 70.6   | <0.001  |
| Male         | 54.3%   | 33.6%  | 0.004   |
| Ref error(D) | - 3.02  | - 0.61 | 0.003   |
| Choroidals   | 21%     | 52.4%  | <0.001  |

# TREATMENT OUTCOMES IN THE TUBE VERSUS TRABECULECTOMY (TVT) STUDY AFTER FIVE YEARS OF FOLLOW-UP

Steven J. Gedde, M.D.  
Bascom Palmer Eye Institute



# Treatment Outcomes

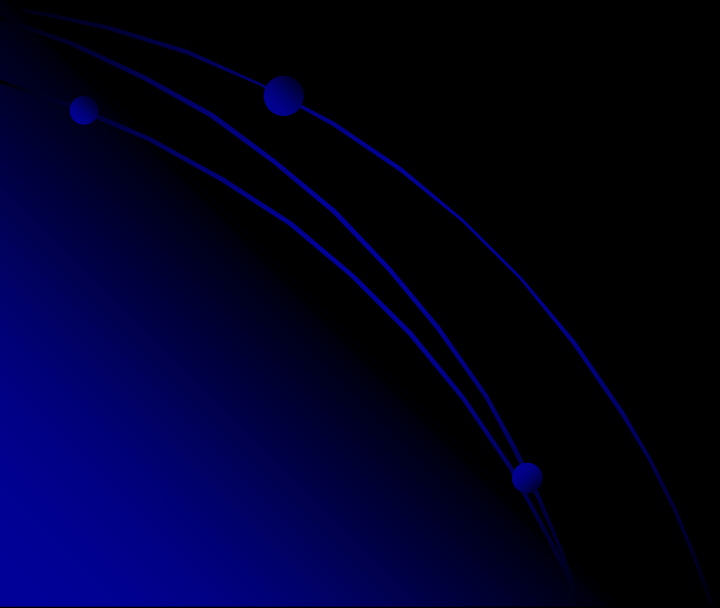
|                  | <b>Tube<br/>Group<br/>(n = 73)</b> | <b>Trabeculectomy<br/>Group<br/>(n = 84)</b> | <b>P-<br/>value</b> |
|------------------|------------------------------------|--|---------------------|
| <b>Failure</b>   | <b>24 (33%)</b>                    | <b>42 (50%)</b>                              | <b>0.034</b>        |
| <b>Success</b>   | <b>49 (67%)</b>                    | <b>42 (50%)</b>                              | <b>0.034</b>        |
| <b>Qualified</b> | <b>31 (42%)</b>                    | <b>18 (21%)</b>                              |                     |
| <b>Complete</b>  | <b>18 (25%)</b>                    | <b>24 (29%)</b>                              | <b>0.58</b>         |

# Reasons for Treatment Failure


|                                   | <b>Tube<br/>Group<br/>(n = 24)</b> | <b>Trabeculectomy<br/>Group<br/>(n = 42)</b> |
|-----------------------------------|------------------------------------|--|
| <b>Inadequate IOP<br/>control</b> | <b>20 (83%)</b>                    | <b>28 (67%)</b>                              |
| <b>Persistent hypotony</b>        | <b>3 (13%)</b>                     | <b>13 (31%)</b>                              |
| <b>Loss of LP vision</b>          | <b>1 (4%)</b>                      | <b>1 (2%)</b>                                |

**P = 0.43 for the difference in distribution of reasons for treatment failure**

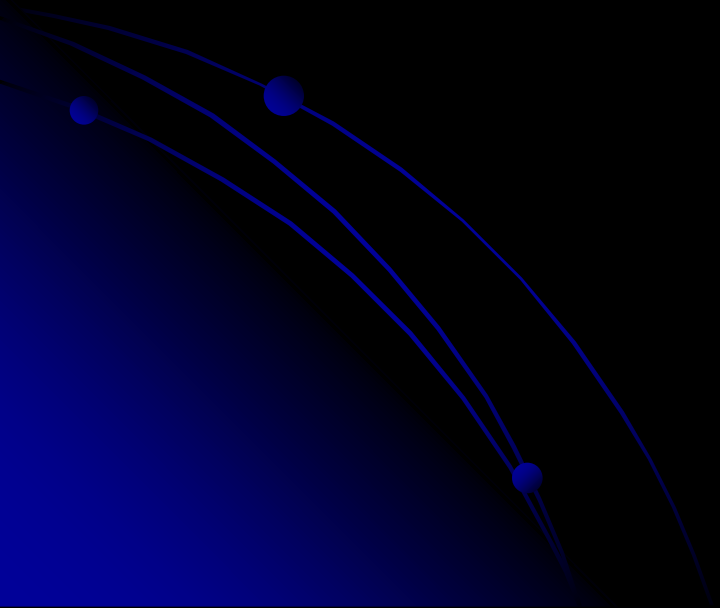
# Collaborative Initial Glaucoma Treatment Study (CIGTS)



# Collaborative Initial Glaucoma Treatment Study

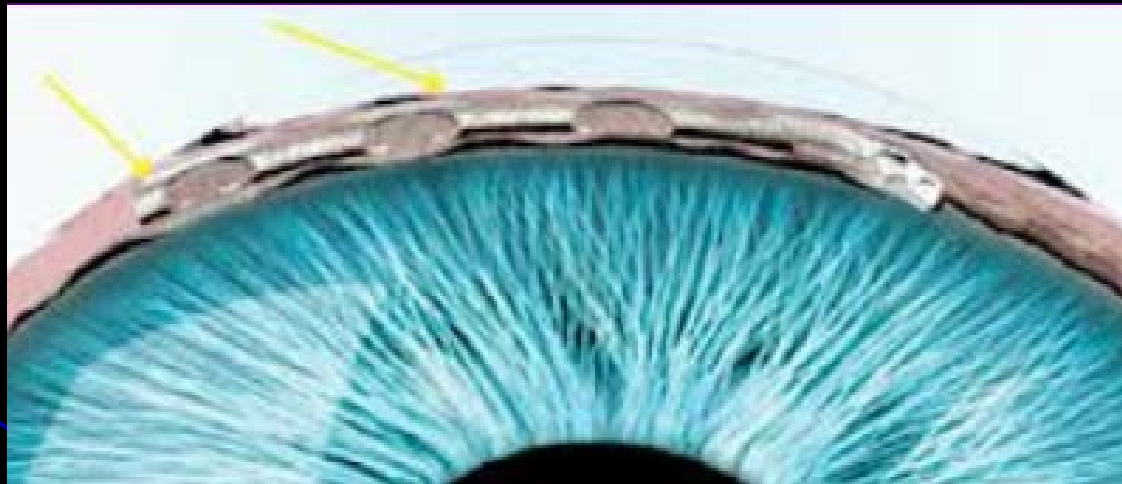
- Hypotony not systematically defined or recorded as postoperative complication on post-trabeculectomy follow-up form
  - Of 465 trabeculectomies performed in study, 4 eyes (0.9%) were described by investigators under “Other Problems” as having “hypotony” or “prolonged low IOP.”
- 

# Trabecular Micro-Bypass Stents





# Intracanalicular MicroStent (Hydrus)



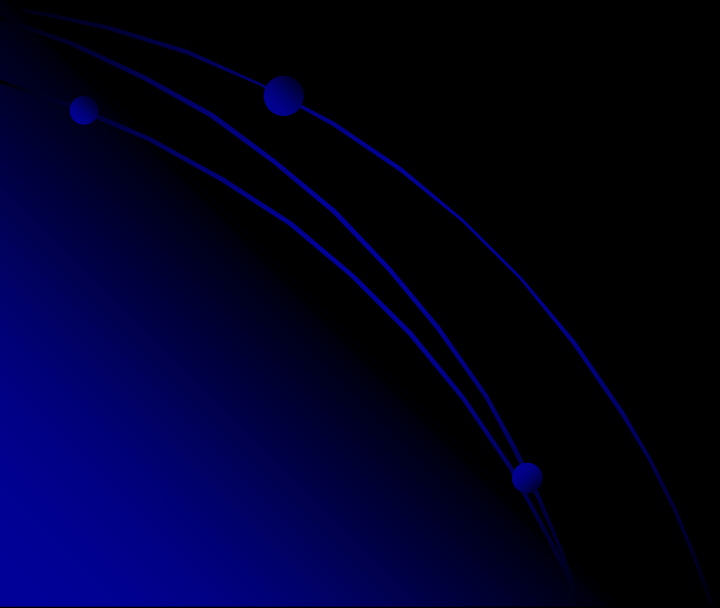
# Trabecular Micro-Bypass Stent (iStent)

- Randomized controlled clinical trial in which 111 patients underwent iStent with cataract surgery and 122 underwent cataract surgery alone
- One eye (group not specified) experienced transient hypotony at 5 – 7 hours that resolved by 1 day postoperatively

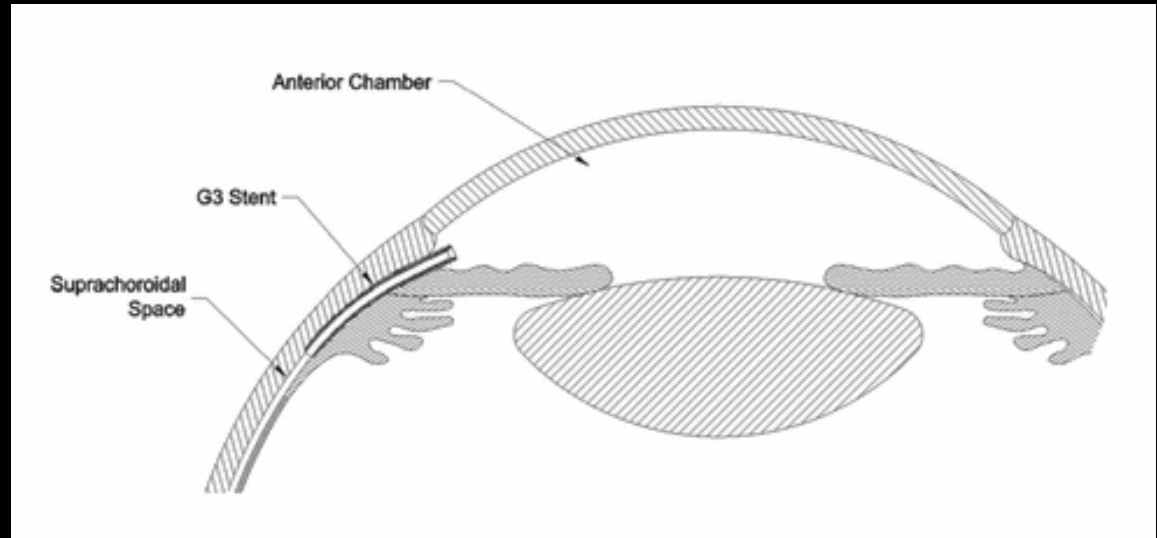
*Samuelson et al, Ophthalmology, 2011*



# Ab-Interno Suprachoroidal Stents



# iStent Supra



*From RA Hill et al, Surgical Innovations in Glaucoma, 2014*

# Suprachoroidal Micro-Stent (CyPass)

- Prospective case series in which 184 patients underwent cataract surgery and placement of suprachoroidal micro-stent
- Most common complication was transient early hypotony ( IOP < 6 mmHg, 25 eyes, 13.8%)
- Hypotony resolved in all but 1 case by 1 month and all cases by 6 months



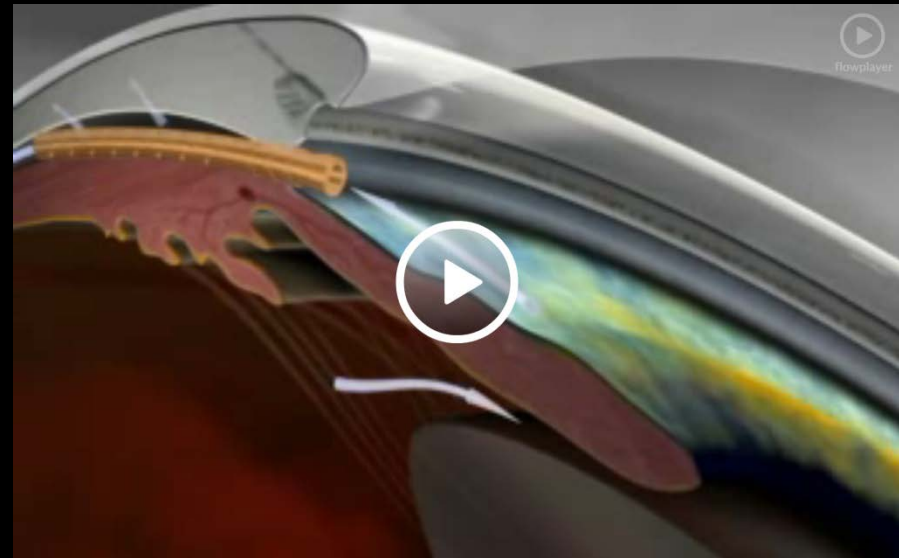
*Hoeh et al, JCRS, 2013*



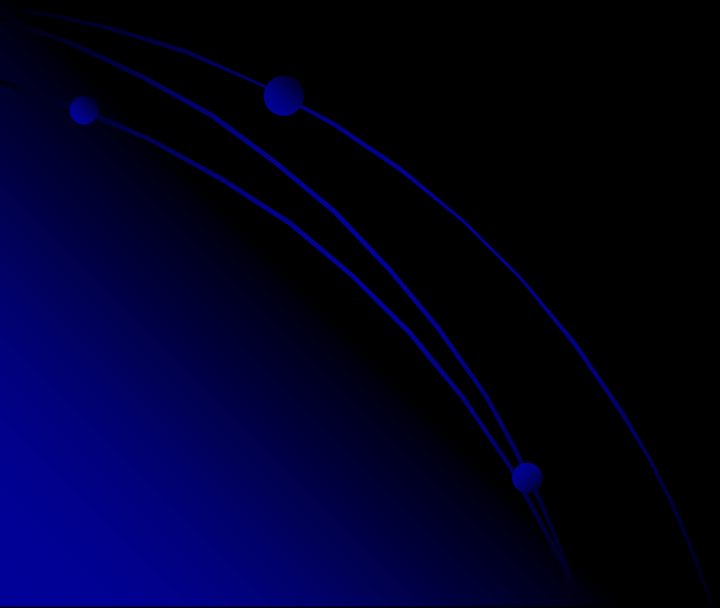
# Suprachoroidal Micro-Stent (CyPass)

- Transient hypotony was attributed to micro-stent placement and creation of cyclodialysis cleft
- Particularly in early postoperative course, cleft may extend beyond implant's external diameter

*Hoeh et al, JCRS, 2013*

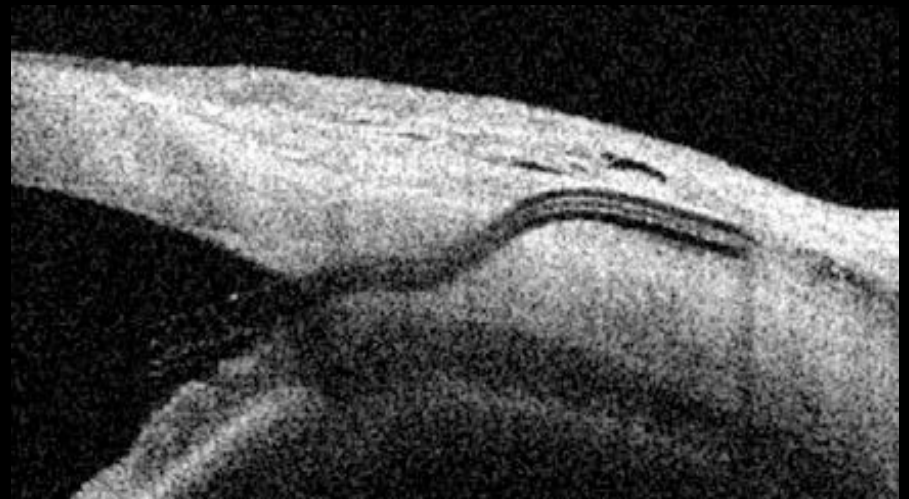


# Subconjunctival-Based Transscleral Filtration Devices



# AqueSys XEN Gel Stent

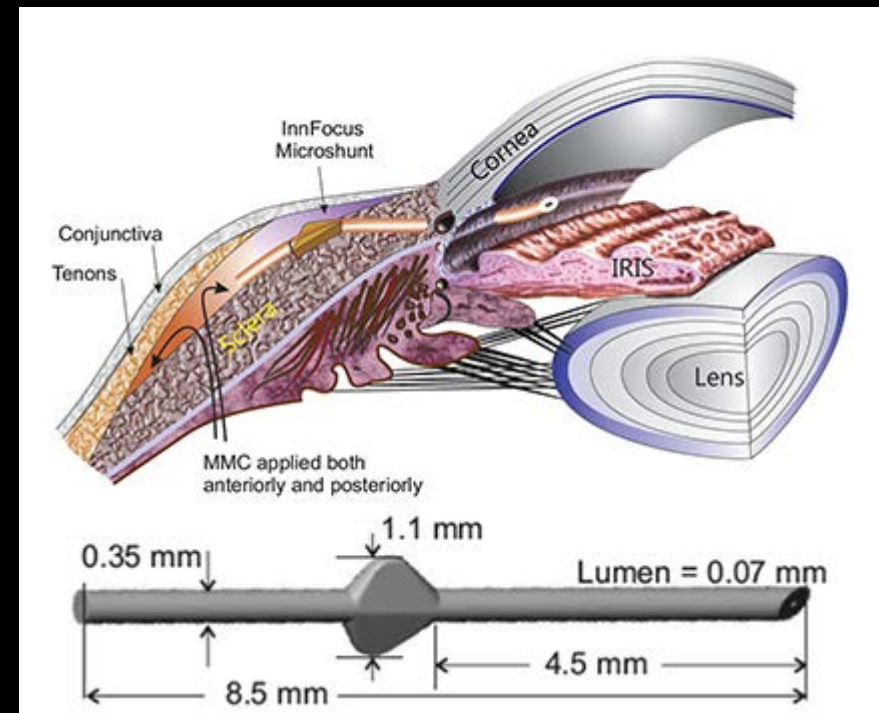
- Soft, collagen-based gelatin implant injected into subconjunctival space by ab interno approach through clear corneal incision
- No peer-reviewed publications to date



*Courtesy Steven R. Sarkisian, Jr., MD*

# InnFocus Microshunt

- Filtering device made from polymer called poly(styrene-block-isobutylene-block-styrene) and placed by ab externo approach
- Procedure involves creation of fornix-based conjunctival flap and use of intraoperative mitomycin
- No peer-reviewed publications to date



# AqueSys XEN Gel Stent and InnFocus Microshunt

- Both involve diversion of aqueous to subconjunctival space and creation of filtering bleb
- InnFocus Microshunt accompanied by use of intraoperative mitomycin
- Both devices attempt to control flow and minimize hypotony by applying Poiseuille's Law of laminar flow to create tube that is sufficiently long and narrow
- As filtering procedures, will be important to determine incidence of transient and long-term hypotony and any impact on vision



# Summary and Conclusions

- Would be helpful and appropriate to establish consistent definition of hypotony
- Documentation of transient and longer term hypotony may be particularly relevant for minimally invasive surgical procedures that involve placement of device into suprachoroidal space or subconjunctival filtration
- Very important to document visual impact, if any, and differentiate postoperative “statistical hypotony” from “clinically significant hypotony”